

Synthetic Organic Chemicals

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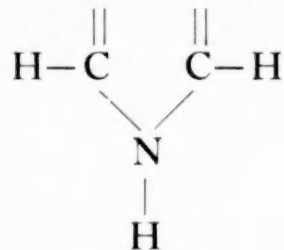
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Pyrrole and Some of its Derivatives

IN recent years the work of Willstätter, Fischer, and others has shown that pyrrole $\text{H}-\text{C}-\text{C}-\text{H}$ is the funda-



mental unit or building stone in those two interesting and vital substances, chlorophyll, the green coloring matter of the plant and vegetable kingdom, and hemoglobin, the red of blood.

Pyrrole, relative to benzene, is a distinctly aromatic compound. And because of the ease with which it can be iodinated, mercureated, etc., it can even be said to have super-aromatic properties. Thus, in a general way, it may be placed with furan and thiophene, which are in many respects the most "aromatic" cyclic compounds known. However, the literature on pyrrole has not as yet been well enough collected to permit broad generalization as to its relative aromaticity in respect to benzene or any other typical aromatic compound. It should also be pointed out that there are marked chemical differences between pyrrole on the one hand and furan and thiophene on the other, even though the three be grouped together because of their super-aromatic properties as compared to benzene.

Pyrrole can be prepared in yields of

25-30% by distilling the ammonium salt of mucic acid from an iron retort. It has been found possible to improve the yield to a maximum of about 50% by mixing the ammonium mucate with glycerine and then distilling. However, it is believed that the first method is superior, for when glycerine is used, frothing will take place.

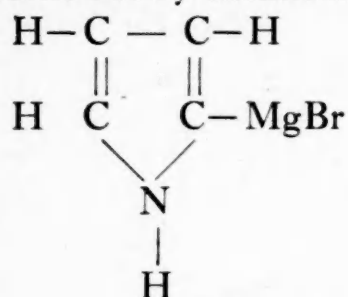
N-Methylpyrrole can be prepared by treating one mole of mucic acid with two of methylamine. The solid, thus obtained, is distilled as described for pyrrole. With the higher N-substituted pyrroles, such as N-butylpyrrole, some prefer to carry out the distillation under reduced pressure. However, equally good yields can be obtained if the mucic acid amine complex is distilled under normal pressure. It is worthy of note that the method described is a general one as CH_3- has been replaced with C_6H_5- , $\text{C}_6\text{H}_5\text{CH}_2-$, $\text{CH}_3\text{C}_6\text{H}_4-$, etc.

When heated in a sealed tube, the N-substituted derivatives of pyrrole rearrange to give the 2-substituted derivatives of pyrrole. Thus, N-ethylpyrrole, when heated, rearranges to 2-ethylpyrrole. It is interesting to note that the N-substituted derivatives of pyrrole, when heated at a temperature higher than that necessary to cause a simple rearrangement, are decomposed to give derivatives of pyridine. In this manner N-benzylpyrrole is decomposed to give 3-phenylpyridine.

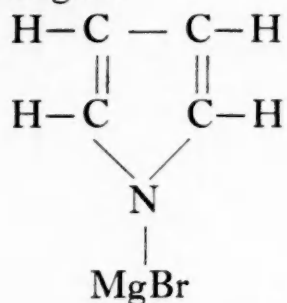
When one mole of pyrrole in an inert solvent (ether) is treated with an atom of potassium, one atom of hydrogen is evolved and N-potassium pyrrole is formed. From this compound it is possible to prepare a multitude of pyrrole derivatives. These include ethyl-N-pyrrole formate, N-ethylpyrrole, N-acetylpyrrole, N-benzylpyrrole, etc.

N-acetylpyrrole, which is a liquid, when heated rearranges to give 2-acetylpyrrole (pyrryl-2-methyl ketone), a solid.

One mole of pyrrole dissolved in ether reacts with slightly more than one mole of ethylmagnesium bromide to give one mole of ethane and pyrrylmagnesium bromide. The constitution of this compound has been the subject of considerable speculation and investigation; the best experimental evidence now available assigns to it the following structure which is borne out by chemical evidence:



It has also been suggested that pyrrylmagnesium bromide may have the following structure because of its one active hydrogen:



Pyrrylmagnesium bromide is a typical nuclear-substituted cyclic Grignard reagent which permits the preparation of an almost endless number of compounds substituted in the 2-position.

Pyrrole is known to react with mercury acetate with comparative ease. The mercury and lead derivatives of pyrrole should prove to be of interest

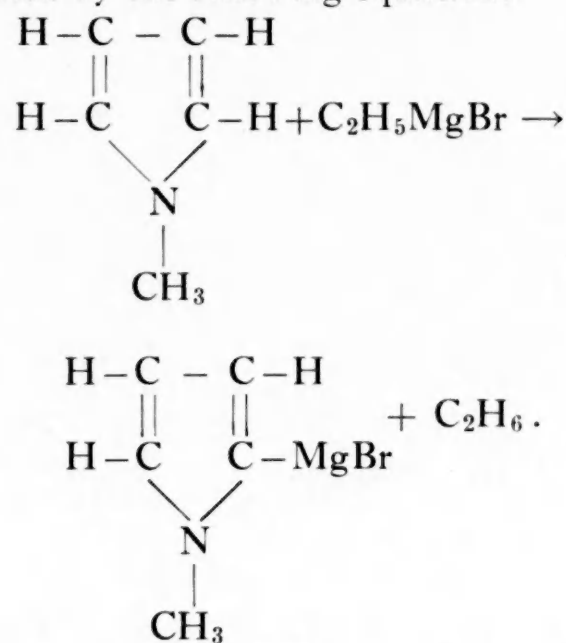
for physiological studies, and to those interested in series of replacements, negativities, reactivities, etc.

Tetraiodopyrrole can be prepared by treating pyrrole with iodine in an alkaline solution. This compound has found use in medicine. The mono-halogenated derivatives of pyrrole can be prepared by treating pyrrylmagnesium bromide with the desired halogen.

A variety of nitropyrroles (probably the 2- and 2.5-substituted compounds) have been prepared by nitrating compounds like pyrryl-2-methyl ketone and pyrryl-2-carboxylic acid. Various isomeric di-substituted nitropyrroles have been reported. It is possible to reduce the nitro derivatives of pyrrole to the corresponding amino compounds.

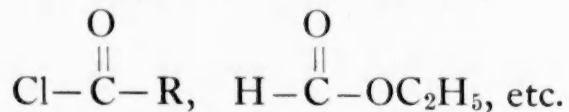
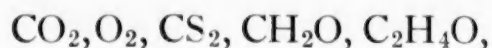
Pyrrole and its N- and 2-substituted alkyl and aryl derivatives can be reduced to the corresponding pyrrolidine compounds by means of Adams' platinum oxide catalyst in alcohol acidified with hydrogen chloride.

N-Methylpyrrole, when treated with ethylmagnesium bromide, reacts as indicated by the following equation:



The N-methylpyrryl-2-magnesium bromide thus formed should react as does a normal nuclear-substituted cyclic Grignard reagent. It is not beyond the realm of possibility, however, that this compound, as well as pyrrylmagnesium

bromide itself, would react *abnormally* or not at all with so-called typical reactants:



The pyrrole ring can be opened with comparative ease. An example is the reaction between 2.5-diethylpyrrole and hydroxylamine in alkaline solution to form the dioxime of 3.6-diketo-octane. If the ethyl groups were replaced with methyl groups, there would result the dioxime of acetyl acetone, which compound can be obtained by the

action of hydrogen chloride and hydrogen cyanide on 2.5-dimethylfuran.

Pyrrole, as well as the following compounds, is made in the Synthetic Chemistry Department of the Kodak Research Laboratories.

Hemin
Proline
N-Benzylpyrrole
N-n-Butylpyrrole
N-Ethylpyrrole
N-Methylpyrrole
N-Phenylpyrrole
N-o-Tolylpyrrole
N-m-Tolylpyrrole
N-p-Tolylpyrrole

B. Coli versus *B. Aerogenes*

IN the bacteriological examination of water, the presence of the coli-aerogenes group as shown by standard tests has been considered evidence of human contamination. Although the colon bacillus is quite definitely an inhabitant of the human intestinal tract, the various strains of aerogenes often may come from sources above suspicion. Unfortunately, the reactions of these two types are very similar and the usual tests do not differentiate between them. Consequently, perfectly good water many times has been condemned as being unfit for use.

In recent years much work has been done in attempting to devise suitable methods for distinguishing between these two types. One of the most successful is the use of cellobiose in the meat extract-peptone broth used in growing the culture. In this broth the aerogenes strains consume the cellobiose with formation of gaseous products and at the same time increase the acidity of the medium. Cultures of *B. Coli* show neither of these reactions.

The test may be carried out in a fermentation tube in order to measure

the gas formation, and, if an indicator is added to the broth, the development of acidity can also be followed by the change in color. Bromcresol purple with a pH range 5.2-6.8 is a satisfactory indicator for this purpose. Incubation under suitable sterile conditions is carried out for approximately forty-eight hours. This method has shown very uniform results both on pure cultures and by comparison with other differentiation tests.

Cellobiose is a disaccharide which may be obtained in the form of its octaacetate by the acetolysis of cellulose. Hydrolysis of the acetate yields the sugar, itself. It is a white, optically active, crystalline powder. Alpha-methylglucoside is another carbohydrate which has been recommended recently for differentiating between cultures of *B. Coli* and *B. Aerogenes*. This sugar derivative is prepared from glucose by treatment with a methyl alcohol solution of hydrogen chloride.

Special grades of cellobiose and alpha-methylglucoside which have been tested for bacteriological work can now be supplied from our stock of Eastman Organic Chemicals.

Forty New Eastman Organic Chemicals

The following chemicals were added to our list during the summer months. Purity specifications and prices of these compounds will be supplied promptly on request.

Allylarsonic Acid
2-Amino-4-chlorothiophenol Hydrochloride
n-Amylbenzene
dl-Asparagine
Benzylarsonic Acid
o-Benzylphenol
Boric Anhydride
o-Bromiodobenzene
m-Chloriodobenzene
o-Chloriodobenzene
p,p'-Difluorodiphenyl
Dihydrazinodiphenyl Dihydrochloride
2,4-Dimethylphenacyl Chloride
2,4-Dinitrophenetole
Ethylarsonic Acid
Ethyl Diselenide
 α -Ethyl- α -phenylhydrazine
p-Fluorobenzoic Acid
 α -Fluoronaphthalene
 α -Furil Dioxime
o-Hydroxyacetophenone
o-Hydroxypropiophenone
p-Hydroxypropiophenone
o-Iododiphenyl
p-Iododiphenyl
Methyl Benzoylacetate
Methyl β -Naphthyl Ketone
 β -Methyl-l-xyloside
m-Nitroacetanilide
o-Nitroacetanilide
p-Nitrobenzamide
p-Nitrobenzonitrile
p-Nitrofluorobenzene
o-Nitrosonitrobenzene
n-Propylarsonic Acid
n-Propylidine Chloride
Quininic Acid
Tetraphenyllead
Thianthrene
Triphenylcarbinol Methyl Ether

Eastman Organic Chemicals as Analytical Reagents

XXVI Reagents for Antimony.

PYROGALLOL

Feigl, Z. ANAL. CHEM. 64, 44 (1924)

In a solution very weakly acid with hydrochloric acid, trivalent antimony forms a white precipitate with pyrogallol. The pyrogallol is added in the solid form and the solution stirred well. Precipitation is not complete in neutral, acetic acid, or alkaline solutions but requires the presence of a small amount of mineral acid. A little tartaric acid may be added to prevent formation of oxychlorides. The reaction is very sensitive and serves also for identifying antimony microchemically.

HEXAMETHYLENETETRAMINE

Vivario and Wagenaar, Z. ANAL. CHEM. 67, 298 (1925)

This reagent reacts with antimony trichloride to give a precipitate of white octahedral crystals suitable for microchemical identification. Sensitivity can be increased by the addition of potassium iodide-iodate. Tin gives crystals having a similar appearance, but the two can be distinguished by the difference in solubility in caesium chloride.

PHENYLTHIOHYDANTOIC ACID

Lassieur, COMPTES-RENDUS 176, 1221 (1923)

The neutral antimony solution is made slightly acid (brom-thymol blue) with acetic acid and treated with a slight excess of solid phenylthiohydantoic acid. The solution is boiled 5 or 6 minutes and then thoroughly cooled. The voluminous white precipitate formed is filtered through a Gooch crucible and washed with a little cold water. It is then taken up in hot alcohol, re-precipitated as the sulfide, and finally determined electrolytically.